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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 02/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,694	ADAMS ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,164 and 485-520* is/are pending in the application.

4a) Of the above claim(s) *485-500,507 and 508* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,164,501-506 and 509-520* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 1/9/06, claims 13 and 164 have been characterized as amended. Claims 485-520 have been added. In addition, the following claims have been cancelled: claims 1-12, 40, 44, 61, 77, 94, 112, 129, 172, 192, 198, 267, 276, 281, 283, 287, 290, 294, 299, 309, 362-364, 405, 437, 467.

Claims 13, 164, and 485-520 are now pending.

✧

Applicants' additional species elections are acknowledged.

a) the compound on page 3, line 17+ in which "m" is zero, and the isoleucine is in the "L" configuration;

b) the infectious disease is viral and more specifically influenza;

c) the agent of formula I is administered by injection;

d) the compound of formula I is administered without another active agent being present;

e) an agent of formula I *per se* is not administered; rather, a composition that contains the agent of formula I in combination with a carrier is administered.

It is noted also that applicants have volunteered that the influenza antigen which has infected the elected subject was at one point present within a bacteria. Despite this, none of claims 491-493 encompasses the elected specie, since applicants have opted for administration of a composition in which a second active agent is absent.

Claims 497-500 are withdrawn from consideration. The issue here is that neither the

formulas in question, nor the definitions of the substituent variables are provided in these claims (497-500). It may be the case that these claims will ultimately prove to be subgeneric to claim 13 (or that the scope of the respective genera will coincide exactly). But this cannot be determined at the present time. In the event that claims 497-500 are amended in response to this Office action to make it clear what the formulas are, and how the substituent variables are defined, these claims will be rejoined in the subsequent Office action, if deemed appropriate. (If applicants defer such an amendment, however, the claims may not be rejoined).

Thus, the following claims are withdrawn from consideration, since they do not encompass the elected species: 485-500, 507, 508. Claims 13, 164, 501-506, 509-520 are examined in this Office action.

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35 U.S.C. §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 164, 502, 504, 506, 510, 512, 514, 516, 518, 520 are rejected under 35 USC §101 because the claimed invention is not supported by a well established utility.

The cited claims are drawn to a method of "preventing" an infectious disease. This would mean that not a single virus, bacteria, fungus, parasite or prion can divide or propagate or replicate while present within the subject. For example, suppose that one of the claimed compounds were administered to each of 1000 human subjects, and that each of those 1000 human subjects were were subjected to injections of HIV, influenza virus, anthrax, poxvirus, poliovirus, pneumococcus, and candida. Suppose that of those 1000 persons, 999 exhibited no adverse symptoms of any kind, but that the 1000th person developed a mild cold from which a recovered within a few days. Such a result would be wildly successful by any standard; yet such a result would actually constitute evidence that prevention had not been achieved. Applicants data does not come close to showing that prevention can be achieved.

Claims 164, 502, 504, 506, 510, 512, 514, 516, 518, 520 are also rejected under 35 USC §112 first paragraph. Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

✦

Claims 511-512 are rejected under 35 U.S.C. 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It appears that descriptive support is lacking for the "96%" limitation. Applicants are requested to point to the relevant page and line number.

✦

Claims 13, 164, 501-506, 509-520 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 13 is drawn to a method which calls for administering an "agent" of formula I. How is an "agent" different from a "compound"...? If a compound is intended, this should be made clear. A related issue is that the claim calls for administering an agent of formula I; according to the formula there is no carrier present. At the same time, however, the claim mandates that the agent is administered by injection or in an interically coated form. How do applicants propose to inject a solid compound? If a carrier is present, this should be made clear. (The same issues apply in the case of claim 164).

- Claim 13 recites that the agent is administered in an amount effective to "inhibit" the infectious disease. This is objected to partly on semantic grounds, and partly on scientific grounds. The term "inhibit" applies to a process. One can inhibit a process, but one cannot inhibit a state of being. For example, one could inhibit the formation of rust, but one cannot inhibit the rust itself. One could inhibit the propagation of a virus, but if one has a dormant population of virus particles in a test tube, it would be meaningless to say that one intends to "inhibit" those virus particles. And to the main point, one could (if one were enabled) inhibit one of the biochemical processes which underlies the manifestations of a disease, and one could inhibit the progress of a disease. But to say that one will attempt to "inhibit" a disease is not meaningful. (The same issue applies in the case of claim 164). If there

is descriptive support for the term "replication" or "propagation", following are examples of claim language that could be used:

A method of treating a subject infected with influenza virus comprising administering to said subject a compound of formula I in an amount effective to inhibit replication of the influenza virus

A method of treating a subject infected with influenza virus comprising administering to said subject a composition that comprises a pharmaceutically acceptable carrier and a compound of formula I in an amount effective to inhibit propagation of the influenza virus.

- Claims 13 and 164 are indefinite as to the infectious diseases intended.

- Claim 13 recites (fifth line from last) that substituent variable R "**can be** [an] organoboronate...." . This renders the claim indefinite. This can be interpreted to mean the "R" can be anything and everything. Is this intended? (The same issue applies in the case of claim 164). Similarly, the claim recites that A **may be** ...an amino acid. Does this mean that "A" can be anything?

- Claim 13 makes reference to a variable "Am". This could be interpreted to mean that "m" is a subscript of "R", or that "R" is to be taken "m" times. Clarity would be enhanced by using the denotation $(A)_m$ instead of "Am". (The same issue applies in the case of claim 164).

- Substituent variable "A_1" is recited to be an amino acid, yet in the elected specie, A_1 is not an amino acid, but is rather an amino acid which lacks either a carboxyl group or a carbonyl group. Thus, which controls; does the elected specie fall outside the scope of the elected invention, or is in fact A_1 improperly defined?

- In claim 13, 4th line from last, the following is recited:

  "fluoroolefins dipeptide isoesteres"

  It appears that a comma should be present between "fluoroolefins" and "dipeptide isoesteres" Is this correct?

- In the claims, the term "alphaketo" is indefinite. What is the keto group "alpha" to...? Is it an *alpha*-ketoamide, *alpha*-keto ester, *alpha*-keto phosphonate, *alpha*-keto boronic acid, *alpha*-keto acid, *alpha*-keto phosphate, or something else?

- The claims recite the term "FAP". This term may be used if accompanied by an explanation of its meaning.

- The claims recite the following term:
  N-peptioloyl - O- acylhydroxylamine)
  However, the term " peptioloyl" is misspelled

- Claim 13 recites (second to last line) that "**it** is capable of reacting" .... what is "it"...? Also, the term "capable of reacting" renders the claims indefinite as to whether the reacting ever takes place.

- Claims 511-512 make reference to chirality, reciting that at least 96% of the agent is "L" isomer. The first issue is that claims 13 and 164 are each drawn to <u>one</u> agent, and not a mixture of agents. As such, for the case of "m" being zero the isoleucine would have to be either 100% "D" or 100% "L". One can, of course have a mixture of compounds, but if this is intended, claims 511-512 should be cast in independent form so that this can be made clear. Another issue is that, for the case of "m" being 10, there would be at least 11 chiral centers "in play". To what is the 96% parameter referring in this case?

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The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of

section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 13, 164, 503-506, 509-520 are rejected under 35 U.S.C. §103 as being unpatentable over Priestley (USP 6939854).

Priestley discloses (table 1, col 64) various peptides which comport with the following formula:

Asp-Glu-Val-Xaa-W

wherein

"Xaa" is an amino acid such as ethylglycine or tbutyl-phenethylglycine;

"W" is a substituent variable used in the reference, and represents boronic acid pinanediol ester

Also disclosed is that the peptides can be used to treat hepatitis. Priestly does not disclose that one of the methyl groups of the valine side chain can be be extended by one methylene unit without adverse effect. However, the peptide chemist of ordinary skill would expect that if the side chain of an amino acid is extended by one methylene unit, activity will be substantially retained (*In re Shetty* (**195** USPQ 753); *In re Hass & Susie* (**60** USPQ 544). In other words, the peptide chemist of ordinary skill would expect that if a given peptide containing a

valine exhibits a particular biochemical activity, then an otherwise identical peptide containing an isoleucine (at the position that the valine occupied) will exhibit substantially the same activity.

Given that hepatits is an infectious disease, the claims are rendered obvious.

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Claims 13 & 164 are rejected under 35 U.S.C. §103 as being unpatentable over Wallner (USP 6,355,614).

Wallner discloses that the dipeptide Val-BoroPro can be used to treat HIV infection. In accordance with the discussion above (the §103 over Priestley), the disclosure of Val-BoroPro renders obvious the elected specie (Ile-boroPro).

Thus, the claims are rendered obvious.

✧

References B1, B2 and B3 were stricken from the IDS. The record should be made clear that only the abstracts were considered. It is suggested that the following be cited on the IDS in the "other documents" section (note that an abstract is not a patent):

Abstract of EP 0371467.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800